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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,707	04/02/2004	Alan K. Smith	250512US	9727

22850 7590 06/07/2005

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,707	SMITH ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-77* is/are pending in the application.

4a) Of the above claim(s) *52,53 and 60-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-51 and 54-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 46-77 are pending.

2. Applicant's election with traverse of Group I claims 46-51,54-59 in the reply filed on 04/21/05 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups I-III together would not constitute a serious search burden on the examiner and that search of the claims of Group I would provide useful information for the claims of Group II and Group III.

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in paragraphs 3-5 of the previous Office Action and above

The requirement is still deemed proper and is therefore made FINAL.

Claims 52, 53 and 60-77 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 46-51 and 54-59 read on a composition comprising lineage committed dendritic cells, wherein said cells are antigen primed dendritic cells are under consideration in the instant application.

3. The specification on page 1, line 6 should be amended to reflect the status of the parent 09/893,470 application.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

5. Applicant asserted that an IDS has been submitted with the prior application 09/893,470. However these citations have been crossed out as said references cited in said parent application couldn't be found. Applicant is invited to resubmit such references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

6. It is noted that the Brief Description of the Figures, disclosed Figure 1, panels A-D, Fig.2 panel A-B; Fig.3, panel A-B and Fig.4, panel A-B. There is no said panels in the submitted figures.

7. Claims 48 , 49, 56 and 57 are objected to because of the following informalities: The word "wherein" is missing in the first line after the phrase "The composition of claim 46" or "The composition of claim 54" accordingly.

Appropriate correction is required.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 47 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Dependent claims 47 and 55 both recites "the isolated lineage committed dendritic cells". There is insufficient antecedent basis for this limitation in the claims, since base Claims 46 and 54 do not recite the isolated lineage committed dendritic cells.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 46-51 and 54-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a composition comprising isolated lineage committed dendritic cells exhibiting enhanced biological function , wherein said biological function is *in vitro* stimulating activity, compared to the biological function of the lineage committed dendritic cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium, does not reasonably provide enablement a composition comprising isolated lineage committed dendritic cells exhibiting enhanced *any* biological function , wherein said *any* biological function is performed *in vivo*, compared to the biological function of the lineage committed dendritic cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims as written encompass the genus enhanced biological function of a lineage committed dendritic cells, wherein said function are not even defined in the Specification.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses detailed *in vitro* studies wherein dendritic cells were cultured under very specific growth condition that unexpectedly results in 50 fold greater stimulating activity of said cells in the alloMLR compared to dendritic cells grown under static culture conditions (see example 3 in particular). The Specification defined biological function as " the ability of a cell population to carry outs its biological mission, i.e. to performed its recognized biological purpose *in vivo*". However, it is noted that the specification does not adequately teach how to effectively obtained a composition comprising isolated lineage committed dendritic cells exhibiting enhanced *any* biological function , wherein said *any* biological function is performed *in vivo*, compared to the biological function of the lineage committed dendritic cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium. Moreover, the Specification does not even define what biological function,

besides stimulating activity of dendritic cells *in vitro* would be enhanced. Applicant has not exemplified any *in vivo or in vitro* studies, wherein isolated lineage committed dendritic cells exhibiting enhanced *any* biological function. Moreover, no animals models were used to show that said lineage committed dendritic cells would maintained or preserved its enhanced biological function when administering back into mammals. Peshwa (WO'97/03186) teaches that there appear to be a significant difference in the characteristics of dendritic cells their function and properties (see entire document, page 2 in particular). Engleman (WO 97/22349) teaches that biological function of dendritic cells depends on the tissue from which they were separated and that depending on cultured conditions the function may be different and that *in vitro* data does not always correlates with in vivo studies of human dendritic cells (entire document, page 6 in particular) . In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously *in vitro* but a fairly high portion of them still fail *in vivo*.

Since there is no *in vivo* studies and data in the specification to show the effectively of maintaining or preserving any enhanced biological function of committed dendritic cells, it is unpredictable how to correlate *in vitro* results with *in vivo* use. This, although the Specification describes certain *in vitro* experiments, there is no correlation on this record between *in vitro* experiments and in vivo data of maintaining an enhanced any biological function of committed dendritic cells. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to efficacy in humans or animals (emphasis added). Ex parte Maas, 9 USPQ2d 1746.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed composition comprising isolated lineage committed dendritic cells exhibiting enhanced *any* biological function , wherein said *any* biological function is performed *in vivo*, compared to the biological function of the lineage committed dendritic cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

13. Claims 46, 47, 51, 54, 55 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Smith et al. (Blood, 1997, V.90, NO.10 page 347B).

Smith et al., teach a composition comprising lineage committed human dendritic cells , wherein said cells are antigen primed dendritic cells, exhibiting enhanced biological function *in vitro* as compared to the biological function of the lineage commited dendritic cells cultured ex vivo under condition which do not include replacement of the liquid culture (see entire document). Smith et al., teach a growth condition wherein culture medium is continuously perfused. Smith et al., teach that continues medium perfusion at an innoculum density of 1.6×10^{6} cells/ ml enhanced biological function of harvested dendritic cells.

Claims 47 and 55 are included because the claimed functional limitation would be inherent properties of recited cell composition. It is noted that the recited cells composition and the claimed cells composition were cultured under the same growth condition, thus would inherently have the same functional properties. Since the office does not have a laboratory to test the reference human dendritic cells , it is applicant's burden to show that the reference cells do not have the functional properties as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teaching anticipates the claimed invention.

14. Claims 46, 47, 51, 54, 55 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,99,126.

US Patent '126 teaches a composition comprising lineage committed human dendritic cells , wherein said cells are antigen primed dendritic cells, cultured ex vivo under condition wherein the liquid cultured medium is replaced (see entire document, column 13, lines 10-25, column 15, line 54-65 and column 21, line 29-35 in particular. US Patent '126 teachers that media replaced every other day for about $5x10^5$ cells/ml culture(see column 17, lines 60-65 and Example 1 in particular). It is noted that US Patent '126 teaches does not explicitly teaches that said cells have an enhanced biological function as compared to the function of the lineage committed cell cultured *ex-vivo* under conditions which do not include replacement of the liquid culture. However, it is noted that the referenced cells were obtained from the same sources and cultured under the same culturing conditions as claimed thus inherently would have an enhanced biological function *in vitro*. Discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed.

Claims 47 and 55 are included because the claimed functional limitation would be inherent properties of recited cell composition. It is noted that the recited cells composition and the claimed cells composition were cultured under the same growth condition, thus would inherently have the same functional properties. Since the office does not have a laboratory to test the reference human dendritic cells , it is applicant's burden to show that the reference cells do not have the functional properties as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teaching anticipates the claimed invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 46, 48-50, 54 and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al.

The teaching of Smith et al., has been discussed, supra.

The claimed invention differs from the reference teaching in that the Smith et al., does not explicitly teach that the culture medium is replaced daily at the rate of at least 25%, or 50% or 25 to 100% .

It is noted however, that Smith et al., teach a culturing condition, wherein the medium is continuously perused. In other words, Smith et al., teach the culturing condition wherein culture medium is continuously replaced. Moreover, Smith et al further teach that said continuously perused system was set to evaluate the effects of frequent medium exchange on dendritic cell expansion and biological function. It would be conventional and within the skill of the art to determine the optimum rate of replacement of the medium that will result in enhanced biological function of cultured committed dendritic cells. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Thus, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

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